1010/16104-US4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Howard L. WEINER et al.

Serial No: 08/279,275 Group Art Unit: 1818

Filed: July 22, 1994 Examiner: P. Achutamurthy

For: **TREATMENT OF AUTOIMMUNE DISEASE BY ORAL ADMINISTRATION OF AUTOANTIGENS**

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In order to comply with discretionary regulations 37 CFR §§ 1.97 and 1.98, attached hereto is Form PTO-1449, and copies[1] of the documents listed thereon.

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[1]To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated therebetween; if no such English language equivalent is cited, then none is known to the undersigned.

The documents enclosed relate to results obtained from a phase III clinical trial for treatment of multiple sclerosis by oral administration of bovine myelin. They are as follows:

1. A press release issued by AutoImmune Inc. on April 21, 1997 stating "AutoImmune Inc. today announced that preliminary analysis of its Phase III trial for Myloral showed no difference in response between active treatment and placebo." "Myloral" is bovine myelin.

2. A graph comparing the annual attack rate before and after treatment in the Phase III clinical trials of four multiple sclerosis drugs. Three of these drugs, Betaseron, Avonex, and Copaxone, have been approved for sale in the United States. The graph shows that the annual attack rate for multiple sclerosis patients who received Myloral in the AutoImmune Phase III clinical trial decreased substantially, as it did in clinical trials of the three approved drugs. In the Myloral trial, however, the patients receiving placebo experienced a similar decrease in annual attack rate, while patients receiving placebo in the other three trials did not experience as great a decrease.

The strong placebo effect in the Myloral study, as compared with the other studies, is believed to be attributable to the fact that Myloral has no side effects, while the other three drugs do have side effects. Specifically, patients on placebo in the Myloral study had no basis upon which to ascertain whether they were receiving Myloral or placebo, while patients on placebo in the other studies could often tell they were not receiving any drug because of the absence of side effects. Thus, the strong placebo effect in the study of bovine

myelin (Myloral) may have masked beneficial effects that resulted from bovine myelin administration. Thus, the results of this phase III study, while disappointing as a basis for a Phase III FDA submission, are believed to be consistent with encouraging clinical results that have been previously submitted in this application.

3. A table of preliminary "MRI Lesion Load" results for patients enrolled in the phase III study of bovine myelin. This table establishes that a group of multiple sclerosis patients who received bovine myelin (termed "DR2 Positive Males") exhibited a statistically significant difference in "MRI Lesion Load" as compared with similarly afflicted patients who had received placebo. MRI (Magnetic Resonance Imaging) is a test that is used to diagnose multiple sclerosis. "MRI Lesion Load" measures damage to brain tissue that results from that disease. MRI lesion data have been relied on by others in this field as evidence of efficacy in treating multiple sclerosis (MRI lesion data were submitted to the FDA by Chiron Corp. as evidence of the efficacy of Betaseron).

The preliminary numerical results shown in the table indicate the average cubic millimeters of lesions measured in patients of a particular "Patient stratum". During the Phase III trial, DR2 positive males with active multiple sclerosis (i.e., "with at least one Confirmed Attack") who received Myloral exhibited an average increase of 356 cubic millimeters of lesions, as compared to an increase of 3459 cubic millimeters for a similar group on placebo. This result is at a statistically significant level. These results are believed to be consistent with the encouraging clinical results that are already of record in this application.

This Information Disclosure Statement should be considered by the Office under 37 CFR § 1.97(c). A petition under 37 CFR § 1.97(d)(2) and a certification under 37 CFR § 1.97(e) accompany this paper.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,

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